REMARKS

Claims 1-5, 7, 9-12, 25-28, 48 and 51-54 are pending in the subject application. Applicants have hereinabove amended claims 9, 12, 53 and 54, added new claims 55-60 and canceled claim 1-5, 7, 11, 25-28, 48, 51 and 52 without disclaimer or prejudice to applicants' right to pursue the subject matter of these claims in the future. Support for the amendments to the claims may be found, *inter alia*, in the specification as follows: claim 9: page 11, line 9 and lines 23 to 25; page 10, lines 26 to 29, and page 15, line 4; claim 12: page 11, lines 23-28; claim 53: page 16, lines 21-31; claim 54: has been amended to recited proper antecedent from claim 9 and to change claim dependency. Support for new claims 55-60 may be found in the specification, *inter alia*, as follows: claim 55: page 13, lines 14-15; claim 56: page 6, lines 8-7; claim 57: page 15, lines 15-19; claim 58: page 15, lines 19-20; claim 59: original claim 48; and claim 60: page 24, lines 13-15. Upon entry of this Amendment, claims 9, 10, 12, 53 and 54, as amended, and new claims 55-60 will be pending and under examination.

Rejections 35 USC §103

The Examiner maintained the rejection of claims 1-5, 7, 9-12, 25-28, 48, 51-54 as filed on July 7, 2009 under 35 U.S.C. 103(a) as allegedly unpatentable over Katz et al., previously cited, Akanbi et al., previously cited, Hedrick et al., previously cited, Haynesworth et al., previously cited, Tremain et al., previously cited, Djian et al., previously cited, Young et al., previously cited, and Didinsky et al., newly cited.

In response, applicants respectfully traverse the Examiner's ground of rejection. Nevertheless, without conceding the correctness of the rejection, claims 9, 12, 53 and 54 have been amended and claims 1-8,

11, 25-28, 48, 51 and 52 have been canceled without disclaimer or prejudice. None of the pending claims are directed to isolated stem cells.

Applicants' claimed invention, as recited in independent claim 9, is directed to a cell population consisting essentially of adult multipotent human stem cells, which population is either in a quiescent state or requires growth factor to proliferate beyond 70% confluence, and wherein each of said adult multipotent human stem cell has a capacity for self-renewal preserved for at least 130 population doublings, and stably exhibits the following phenotype *in vitro*:

- HLA Class I negative,
- an endogenous telomerase activity of at least 20% of the telomerase activity of the HEK293T transformed cell line,
- a normal karyotype, and
- a degree of senescence of less than 0.05% at 60 population doublings.

Applicants' claimed cell population is thus a homogenous cell population, consisting essentially of adult multipotent human stem cells which have a stable phenotype, the population being either quiescent or proliferating in an undifferentiated state, but being unable to proliferate beyond 70% confluence in the absence of a growth factor. The cell population thus consists essentially of stem cells which have undergone at least 50 to 80 population doublings (see the specification at page 10, lines 2-19) and is in a quiescent or post-quiescent state.

a) A stable stem cell population in a quiescent or post-quiescence stage

Applicants' claimed cell population is different from the cell

population disclosed in Katz.

Katz discloses a first heterogeneous cell population (see Katz, Example 1) which is cultured until near confluence in a medium free of growth factors (page 17, lines 36 to 37 and page 18, line 28, page 19, lines 5 and 12). This population is not a homogeneous population as required by the present claims. Further, it proliferates to near confluence in a medium which contains no growth factors. It is therefore also neither quiescent nor requires growth factor to proliferate beyond 70% confluence.

Katz discloses a second population (See Katz, Example 3) which is clonal, and which can be cultured until 80 to 90% confluent in a medium which does not contain growth factors (Katz, page 20, lines 2 to 5). After transfer to different dishes, the cells are grown until close to confluence and are cultured for more than 15 passages in cloning medium in the undifferentiated state (Katz, page 20, lines 5 to 11). The cloning medium contains no growth factors. This population is not a population as required by the present claims since it is in a state of proliferation and proliferates to near confluence in a medium which contains no growth factors. It is therefore neither quiescent nor requires growth factor to proliferate beyond 70% confluence. Katz therefore does not disclose cell populations according to the present claims.

Applicants' claimed cell populations are either in a quiescent (non-proliferating, non-senescent) state or alternatively in a post-quiescent, proliferating state. Quiescence is a particular characteristic of stem cells (see the present application page 15, line 6), and can be maintained for highly extended periods. The quiescent state of the claimed cells indicates that the population consists essentially of stem cells, because the limited life-span of non-stem precursor cells means that the non-stem cells have already

died when quiescence is reached (see the present application page 10, lines 1 to 5). Quiescence permits the cell population to be maintained in vitro almost indefinitely. After quiescence has been reached, intense proliferation in the undifferentiated state can be induced by addition of a growth factor, particularly bFGF, allowing large quantities of undifferentiated stem cells to be produced, which is the aim behind the present invention. Such an intense proliferation cannot be carried out prior to quiescence because, as pointed out in the present application (page 12, lines 1 to 7), use of growth factors prior to quiescence has the effect of increasing the precursor/stem cell ratio which is the very opposite of the effect sought.

The advantageous effect of obtaining a quiescent population or a post-quiescent, proliferating population is not obvious over the cited art. Katz makes no attempt to obtain such a population, and does not disclose or suggest that this measure would both eliminate non-stem precursors and allow intense proliferation of undifferentiated stem cells.

Moreover, the cited art provides no motivation to carry out such proliferation. Indeed, Zuk, previously cited by Examiner, also discloses isolation of stem cells from adipose tissue of adults. Zuk states that adipose tissue is an ideal source of stem cells because it obviates the need for extensive expansion of cells after isolation (Zuk, page 212, abstract). Thus given the teaching of Zuk, the skilled person would consider it is not necessary to expand adipose derived stem cells before inducing differentiation. In fact Zuk actually teaches away from expanding the cells for a high number of population doublings because Zuk also discloses that the cells become senescent after passage 15 (Zuk, page 217).

Thus, based on what was known at the time of the invention on adipose derived stem cells, the skilled person would not have expanded the

cells for over 50 population doublings before inducing differentiation. He would thus not have obtained a cell population consisting essentially of stem cell which are in a quiescent state or beyond quiescence. He would thus not have obtained applicants' claimed cell population.

b) Proliferation potential

Applicants' claimed cell population consists essentially of stem cells which can undergo at least 130 population doublings. In this respect, it is noted that this high proliferation potential can be explained by the fact that the claimed cell population is derived from adipose tissue of a child under 10 years old. The obtained stem cells are thus "younger" than stem cells obtained from an "adult". It has now been established that these "younger" stem cells differ from "older" stem cells obtained from an adult in that their telomers are longer, which means their proliferation potential is much higher than that of "older" stem cells.

As previously established, the stem cells disclosed in Katz are obtained from adipose tissue of adults. Their life span is thus shorter than that of the claimed stem cells.

Applicants' claimed cell population thus differs from the cell population disclosed in Katz in that it has a longer lifespan.

The correlation between the age of the donor and the telomere length was not known at the time of the invention. The skilled person could thus not derive from the prior art the teaching that obtaining stem cells from a child donor would increase the life span of the stem cell population.

In conclusion, it is respectfully submitted that applicants' claimed

cell population is not obvious over the cited art for the reasons detailed herein. Accordingly, applicants respectfully solicit a Notice Of Allowance.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone him at the number provided below.

No fee, other than the enclosed $1,110.00 fee for a three-month extension, is deemed necessary in connection with the filing of this Amendment. Authorization is given by the undersigned to charge this amount to Deposit Account No. 03-3125. However, if any additional fee is required, authorization is hereby given to charge the amount of such additional fee to Deposit Account No. 03-3125.

Respectfully submitted,

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